

What is claimed is:

1. A method of normalizing genetic data for n loci, wherein n is an integer greater than one, comprising
 - 5 (a) obtaining genetic data comprising n sets of first and second signal values related in a coordinate system, wherein said first and second signal values are indicative of the levels of a first and second allele, respectively, at n loci;
 - (b) identifying a set of sweep points in said coordinate system;
 - 10 (c) identifying a set of control points, said control points comprising at least a subset of said signal values that are proximal to said sweep points;
 - (d) determining parameters of a registration transformation equation based on said set of control points; and
 - (e) transforming said n sets of first and second signal values according to said registration transformation equation and said parameters, thereby 15 normalizing said genetic data.
2. The method of claim 1, wherein said genetic data is represented in a graphical format.
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3. The method of claim 2, wherein said graphical format comprises Cartesian coordinates.
4. The method of claim 1, wherein said genetic data is provided in a tabular format.
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5. The method of claim 1, wherein n is at least 2.
6. The method of claim 1, wherein said identifying sweep points comprises

- (i) identifying an upper limit on a line or curve through said coordinate system;
and
- (ii) locating said sweep points between the origin of each axis and said upper limit.

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7. The method of claim 6, wherein said upper limit has a value in a first dimension that is greater than or equal to the first dimension of any of said signal values.

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8. The method of claim 6, further comprising a step of identifying a lower limit on said line or curve, and wherein said locating comprises locating said sweep points between said lower limit and said upper limit.

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9. The method of claim 1, wherein said identifying a set of control points comprises triangulation using pairs of signal values and a sweep point.

10. The method of claim 9, wherein said triangulation comprises Delaunay triangulation.

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11. The method of claim 1, wherein said identifying a set of control points comprises computing all pair-wise distances between the signal values and each sweep point.

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12. The method of claim 1, wherein said determining parameters of a registration transformation equation comprises projecting said control points to a line or curve passing through said sweep points, thereby forming set points.

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13. The method of claim 12, wherein said registration transformation equation comprises affine transformation projecting said control points onto said set points.

14. The method of claim 12, wherein said registration transformation equation comprises linear conformational transformation projecting said control points onto said set points.

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15. The method of claim 12, wherein said registration transformation equation comprises projective transformation projecting said control points onto said set points.

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16. The method of claim 12, wherein said registration transformation equation comprises polynomial transformation projecting said control points onto said set points.

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17. The method of claim 1, wherein said determining parameters of a registration transformation equation comprises global registration.

18. The method of claim 1, wherein said set of control points is fewer in number compared to the number of first and second signal values.

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19. The method of claim 1, wherein said sweep points are located on a line or curve through said coordinate system when represented graphically.

20. The method of claim 19, wherein said line comprises an axis of said coordinate system.

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21. The method of claim 1, wherein said sweep points are spaced along said line or curve in a manner selected from the group consisting of linear, log-linear and non-linear.

22. The method of claim 1, wherein said coordinate system comprises two dimensions.

23. The method of claim 22, wherein step (b) comprises identifying two sets 5 of sweep points in said coordinate system; and step (c) comprises identifying two sets of control points.

24. The method of claim 1, wherein said genetic data comprises n sets of first, second and third signal values related in a coordinate system, wherein said first, 10 second and third signal values are indicative of the levels of a first, second and third allele, respectively, at n loci.

25. The method of claim 24, wherein said coordinate system comprises three dimensions.

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26. The method of claim 24, wherein step (b) comprises identifying three sets of sweep points in said coordinate system; and step (c) comprises identifying three sets of control points.

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27. The method of claim 1, wherein said registration transformation is selected from the group consisting of rotation of said n sets of first and second signal values, translation of said n sets of first and second signal values, scaling of said n sets of first and second signal values, and sheer of said n sets of first and second signal values.

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28. The method of claim 1, further comprising a step of balancing said n sets of first and second signal values by a signal transformation, thereby balancing the probability function for the distribution of said n sets of first and second signal values as a function of signal intensity.

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29. The method of claim 1, wherein said signal transformation is selected from the group consisting of natural logarithm, base 2 logarithm, base 10 logarithm, arctangent, square root, nth root, wherein $n > 2$, and Box-Cox.

5 30. A method of clustering genetic data for n loci, wherein n is an integer greater than one, comprising

- (a) obtaining genetic data comprising n sets of first and second signal values related in a coordinate system, wherein said first and second signal values are indicative of the levels of a first and second allele, respectively, at n loci;
- (b) comparing fit of said genetic data to each of a plurality of cluster models using an artificial neural network, thereby determining a best fit cluster model; and
- (c) assigning said signal values to at least one cluster according to said best fit cluster model.

10 31. The method of claim 30, wherein if said best fit cluster model contains at least one actual cluster and at least one missing cluster, then using a second artificial neural network to propose a location for said at least one missing cluster.

15 20 32. The method of claim 30, wherein said plurality of cluster models comprises at least seven cluster models.

25 33. The method of claim 30, further comprising training said first or second artificial neural network with an algorithm selected from the group consisting of a genetic algorithm, back-propagation algorithm, Levenberg-Marquardt algorithm and Bayesian algorithm.

34. The method of claim 30, wherein said first or second artificial neural network comprises a 3 layer feed-forward artificial neural network or a two layer artificial neural network.

5 35. The method of claim 30, wherein said coordinate system comprises two dimensions.

10 36. The method of claim 35, wherein step (c) comprises assigning said signal values to at least one cluster according to said best fit cluster model, wherein if said best fit cluster model contains at least one actual cluster and fewer than three actual clusters, then using a second artificial neural network to propose a location for at least one missing cluster, wherein the sum of actual and missing clusters is three.

15 37. The method of claim 36, wherein if said best fit cluster model contains one actual cluster, then using said second artificial neural network to propose a location for two missing clusters.

38. The method of claim 37, further comprising separately training said artificial neural network for proposing locations for said two missing clusters.

20 39. The method of claim 36, wherein if said best fit cluster model contains two actual clusters, then using said second artificial neural network to propose a location for one missing clusters.

25 40. The method of claim 30, wherein said genetic data comprises n sets of first, second and third signal values related in a coordinate system, wherein said first, second and third signal values are indicative of the levels of a first, second and third allele, respectively, at n loci.

41. The method of claim 40, wherein said coordinate system comprises three dimensions.

42. The method of claim 41, wherein step (c) comprises assigning said signal values to at least one cluster according to said best fit cluster model, wherein if said best fit cluster model contains at least one actual cluster and fewer than six actual clusters, then using a second artificial neural network to propose a location for at least one missing cluster, wherein the sum of actual and missing clusters is six.

10 43. The method of claim 30, wherein said genetic data is represented in a graphical format.

44. The method of claim 43, wherein said graphical format comprises Cartesian coordinates.

15 45. The method of claim 30, wherein said genetic data is provided in a tabular format.

20 46. The method of claim 30, wherein n is at least 2.

25 47. A genotyping system, comprising
(a) an array reader configured to detect signals from separate locations on an array substrate;
(b) a computer processor configured to receive signal values from said array reader;
(c) a normalization module comprising commands for
(i) reading said signal values;
(ii) identifying a set of sweep points for said signal values in a coordinate system;

(iii) identifying a set of control points, said control points comprising at least a subset of said signal values that are proximal to said sweep points;

(iv) determining parameters of a registration transformation equation based on said control points; and

(v) transforming said signal values according to said registration transformation equation and said parameters, thereby providing normalized genetic data; and

(d) a clustering module comprising commands for

(i) reading said normalized genetic data;

(ii) comparing fit of said normalized genetic data to each of a plurality of cluster models using an artificial neural network, thereby determining a best fit cluster model; and

(iii) assigning said signal values to at least one cluster according to said best fit cluster model, wherein if said best fit cluster model contains at least one actual cluster and at least one missing cluster, then using a second artificial neural network to propose a location for said at least one missing cluster.

20 48. A method of determining a genotype score, comprising

(a) obtaining genetic data comprising n sets of first and second signal values related in a coordinate system, wherein said first and second signal values are indicative of the levels of a first and second allele, respectively, at n loci;

25 (b) identifying a set of sweep points in said coordinate system;

(c) identifying a set of control points, said control points comprising at least a subset of said signal values that are proximal to said sweep points;

(d) determining parameters of a registration transformation equation based on said set of control points; and

- (e) transforming said n sets of first and second signal values according to said registration transformation equation and said parameters, thereby normalizing said genetic data;
- 5 (f) comparing fit of said normalized genetic data to each of a plurality of cluster models using an artificial neural network, thereby determining a best fit cluster model;
- 10 (g) assigning said signal values to at least one cluster according to said best fit cluster model, wherein if said best fit cluster model contains at least one actual cluster and at least one missing cluster, then using a second artificial neural network to propose a location for said at least one missing cluster; and
- (k) determining, for an individual, the alleles present at said n loci.